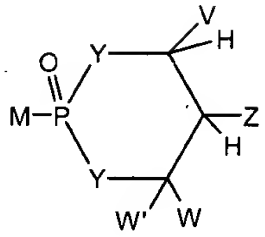
We Claim:

1. A compound of formula I:



I

wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$,

$-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2{}_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2{}_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NH$aryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is independently selected from the group consisting of -O-, $-NR^6-$ with the proviso that at least one Y is $-NR^6-$;

M is selected from the group that attached to $PO_3{}^{2-}$, $P_2O_6{}^{3-}$, $P_3O_9{}^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

1) M is not –NH(lower alkyl), -N(lower alkyl)$_2$, -NH(lower alkylhalide), –N(lower alkylhalide)$_2$, or –N(lower alkyl) (lower alkylhalide); and

2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

2. The compounds of claim 1 wherein $MP(O)(NHR^6)O^-$, $MPO_3{}^{2-}$, $MP_2O_6{}^{3-}$, and $MP_3O_9{}^{4-}$ is selected from the group consisting of an antiviral, anticancer, antihyperlipidemic, antifibrotic, and antiparasitic agents.

3. The compound of claim 1 wherein $MP(O)(NHR^6)O^-$, $MPO_3{}^{2-}$, $MP_2O_6{}^{3-}$, and $MP_3O_9{}^{4-}$ is selected from the group consisting of metalloprotease inhibitor, and TS inhibitor.

4. The compounds of claim 2 wherein MH is selected from the group consisting of LdC, LdT, araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L-FddC, L-d4C, L-Fd4C, 3TC, ribavirin, penciclovir, 5-fluoro-2'-deoxyuridine, FIAU, FIAC, BHCG, 2'R,5'S(-)-1-[2-(hydroxymethyl)oxathiolan-5-yl]cytosine, (-)-b-L-2',3'-dideoxycytidine, (-)-b-L-2',3'-dideoxy-5-fluorocytidine, FMAU, BvaraU, E-5-(2-bromovinyl)-2'-deoxyuridine, Cobucavir, TFT, 5-propynyl-1-arabinosyluracil, CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC, 5-yl-carbocyclic 2'-deoxyguanosine, Cytallene, Oxetanocin A, Oxetanocin G, Cyclobut A, Cyclobut G, fluorodeoxyuridine, dFdC, araC, bromodeoxyuridine, IDU, CdA, F-araA, 5-FdUMP, Coformycin, and 2'-deoxycoformycin.

5. The compounds of claim 2 wherein MH is selected from the group consisting of ACV, GCV, penciclovir, (R)-9-(3,4 dihydroxybutyl)guanine, and cytallene.

6. The compounds of claim 1 wherein MPO_3^{2-} is selected from the group consisting of PMEA, PMEDAP, HPMPC, HPMPA, FPMPA, and PMPA.

7. The compounds of claim 3 wherein M is attached to the phosphorus in formula I via an oxygen atom that is in a hydroxyl group on an acyclic sugar group.

8. The compounds of claim 7 wherein MH is selected from the group consisting of ACV, GCV, 9-(4-hydroxy-3-hydroxymethylbut-1-yl)guanine, and (R)-9-(3,4-dihydroxybutyl)guanine.

9. The compounds of claim 1 wherein M is attached to the phosphorus in formula I via a carbon atom.

10. The compounds of claim 9 wherein $M\text{-}PO_3^{2-}$ is selected from the group consisting of phospohonoformic acid, and phosphonoacetic acid.

11. The compounds of claim 1 wherein $MP(O)(NH\ R^6)O^-$, MPO_3^{2-}, $MP_2O_6^{3-}$, or $MP_3O_9^{4-}$ is useful for the treatment of diseases of the liver or metabolic diseases where the liver is responsible for the overproduction of a biochemical end product.

12. The compounds of claim 11 wherein said disease of the liver is selected from the group consisting of hepatitis, cancer, fibrosis, malaria, gallstones, and chronic cholecystalithiasis.

13. The compounds of claim 12 wherein MPO_3^{2-}, $MP_2O_6^{3-}$, or $MP_3O_9^{4-}$ is an antiviral or anticancer agent.

14. The compounds of claim 11 wherein said metabolic disease is selected from the group consisting of diabetes, atherosclerosis, and obesity.

15. The compounds of claim 11 wherein said biochemical end product is selected from the group consisting of glucose, cholesterol, fatty acids, and triglycerides.

16. The compounds of claim 15 wherein MPO_3^{2-} or $MP(O)(NHR^6)O^-$ is an AMP activated protein kinase activator.

17. The compounds of claim 1 wherein Y is -O- located adjacent to the W' and W groups.

18. The compounds of claim 1 wherein Y is –O- located adjacent to the V group.

19. The compounds of claim 1 wherein both Y groups are $-NR^6-$.

20. The compounds of claim 1 wherein

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy,

alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus.

21. The compounds of claim 20 wherein V is selected from the group consisting of aryl, substituted aryl, heteroaryl, substituted heteroaryl; or

together V and W are connected via an additional 3 carbon atoms to form a cyclic substituted group containing 6 carbon atoms and mono-substituted with a substituent selected from the group consisting of hydroxyl, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy attached to one of said additional carbon atoms that is three atoms from an Y attached to the phosphorus.

22. The compounds of claim 21 wherein V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

23. The compounds of claim 22 wherein Z, W, and W' are H; and R^6 is selected from the group consisting of -H, and lower alkyl.

24. The compounds of claim 23 wherein V is selected from the group consisting of aryl and substituted aryl.

25. The compounds of claim 24 wherein V is selected from the group consisting of phenyl, and substituted phenyl.

26. The compounds of claim 25 wherein V is selected from the group consisting of 3,5-dichlorophenyl, 3-bromo-4-fluorophenyl, 3-chlorophenyl, 3-bromophenyl, and 3,5-difluorophenyl.

27. The compounds of claim 22 wherein V is selected from the group consisting of heteroaryl and substituted heteroaryl.

28. The compounds of claim 27 wherein V is 4-pyridyl.

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29. The compounds of claim 21 wherein together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and mono-substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy attached to one of said additional carbon atoms that is three atoms from an Y attached to the phosphorus.

30. The compounds of claim 29 wherein together V and W form a cyclic group selected from the group consisting of $-CH_2-CH(OH)-CH_2-$, $-CH_2CH(OCOR^3)-CH_2-$, and $-CH_2CH(OCO_2R^3)-CH_2-$.

Sub D9

31. The compounds of claim 1 wherein V is -H, and Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OCOR^3$, and $-CHR^2OCO_2R^3$.

32. The compounds of claim 22 wherein Z is selected from the group consisting of $-OR^2$, $-SR^2$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$.

33. The compounds of claim 32 wherein Z is selected from the group consisting of
$-OR^2$, $-R^2$, $-OCOR^3$, $-OCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$.

34. The compounds of claim 33 wherein Z is selected from the group consisting of $-OR^2$, -H , $-OCOR^3$, $-OCO_2R^3$, and $-NHCOR^2$.

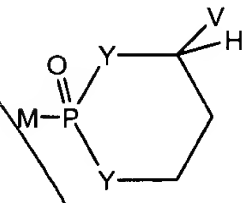
Sub D10

35. The compounds of claim 22 wherein W and W' are independently selected from the group consisting of H, R^3, aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

36. The compounds of claim 35 wherein W and W' are the same group.

37. The compounds of claim 36 wherein W and W' are H.

38. The compounds of claim 20 wherein said prodrug is a compound of formula VI:



VI

wherein

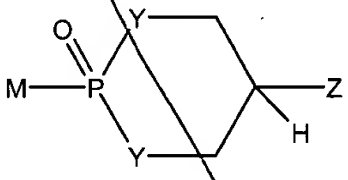
V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

39. The compounds of claim 38 wherein M is attached to phosphorus via an oxygen or carbon atom.

40. The compounds of claim 38 wherein V is selected from the group consisting of phenyl and substituted phenyl.

41. The compounds of claim 38 wherein V is selected from the group consisting of 3,5-dichlorophenyl, 3-bromo-4-fluorophenyl, 3-chlorophenyl, 3-bromophenyl, and 4-pyridyl.

42. The compounds of claim 20 wherein said prodrug is a compound of formula VII:



VII

wherein

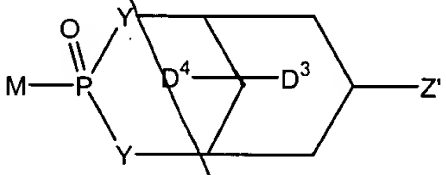
Z is selected from the group consisting of -CHR^2OH, -$CHR^2OC(O)R^3$, -$CHR^2OC(S)R^3$, -$CHR^2OCO_2R^3$, -$CHR^2OC(O)SR^3$, -$CHR^2OC(S)OR^3$, and -CH_2aryl.

43. The compounds of claim 42 wherein M is attached to the phosphorus via a carbon or oxygen atom.

44. The compounds of claim 43 wherein Z is selected from the group consisting of
$-CHR^2OH$, $-CHR^2OC(O)R^3$, and $-CHR^2OCO_2R^3$.

45. The compounds of claim 44 wherein R^2 is -H.

46. The compounds of claim 20 wherein said prodrug is a compound of formula VIII:



VIII

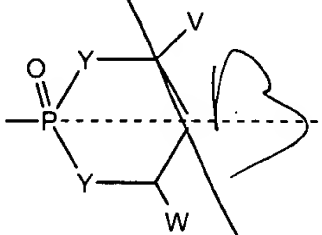
wherein

Z' is selected from the group consisting of -OH, $-OC(O)R^3$, $-OCO_2R^3$, and $-OC(O)S\ R^3$;

D^3 is –H;

D^4 is selected from the group consisting of -H, alkyl, -OH, and $-OC(O)R^3$.

47. The compounds of claim 20 wherein W' and Z are -H, W and V are both the same aryl, substituted aryl, heteroaryl, or substituted heteroaryl, and both Y groups are the same $-NR^6-$, such that the phosphonate prodrug moiety:



has a plane of symmetry through the phosphorus-oxygen double bond.

48. The compounds of claim 32 wherein W and W' are H, V is selected from the group consisting of aryl, substituted aryl, heteroaryl, substituted heteroaryl, and Z is selected from the group consisting of -H, OR^2, and $-NHCOR^2$.

49. The compounds of claim 48 wherein Z is –H, and M is attached to the phosphorus of formula I via an oxygen or carbon atom.

50. The compounds of claim 49 wherein V is selected from the group consisting of phenyl or substituted phenyl.

51. The compounds of claim 49 wherein V is an optionally substituted monocyclic heteroaryl containing at least one nitrogen atom.

52. The compounds of claim 49 wherein M is attached via an oxygen atom.

53. The compounds of claim 51 wherein V is 4-pyridyl.

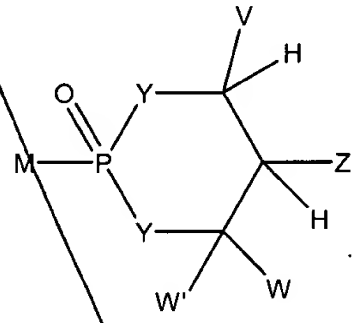
54. The compounds of claim 52 wherein MH is selected from the group consisting of LdC, LdT, araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L-FddC, L-d4C, L-Fd4C, 3TC, ribavirin, penciclovir, 5-fluoro-2'-deoxyuridine, FIAU, FIAC, BHCG, 2'R,5'S(-)-1-[2-(hydroxymethyl)oxathiolan-5-yl]cytosine, (-)-b-L-2',3'-dideoxycytidine, (-)-b-L-2',3'-dideoxy-5-fluorocytidine, FMAU, BvaraU, E-5-(2-bromovinyl)-2'-deoxyuridine, Cobucavir, TFT, 5-propynyl-1-arabinosyluracil, CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC, 5-yl-carbocyclic 2'-deoxyguanosine, Cytallene, Oxetanocin A, Oxetanocin G, Cyclobut A, Cyclobut G, fluorodeoxyuridine, dFdC, araC, bromodeoxyuridine, IDU, CdA, F-ara-A, 5-FdUMP, coformycin, and 2'-deoxycoformycin.

55. The compounds of claim 52 wherein MH is selected from the group consisting of ACV, GCV, 9-(4-hydroxy-3-hydroxymethylbut-1-yl)guanine, and (R)-9-(3,4-dihydroxybutyl)guanine.

56. The compounds of claim 49 wherein M is attached to the phosphorus via a carbon atom.

57. The compounds of claim 56 wherein V is selected from the group consisting of phenyl and 4-pyridyl and MH is selected from the group consisting of PMEA, PMEDAP, HPMPC, HPMPA, FPMPA, and PMPA.

58. A method of enhancing oral bioavailability of a parent drug by administering to an animal a prodrug of formula I:



I

wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy,

alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NH$aryl, $-(CH_2)_p-OR^{12}$, and

$-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is independently selected from the group consisting of –O-, $-NR^6-$ with the proviso that at least one Y is $-NR^6-$;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, $P_3O_9^{4-}$, or $P(O)(NHR^6)O^-$ is a biologically active agent, but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

1) M is not –NH(lower alkyl), $-N(\text{lower alkyl})_2$, -NH(lower alkylhalide), $-N(\text{lower alkylhalide})_2$, or –N(lower alkyl) (lower alkylhalide); and

2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

59. The method of claim 58 wherein M is attached to the phosphorus in formula I via an oxygen atom; wherein

V, W, and W' are independently selected from the group consisting of -H, alkyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl, or

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH{=}CR^2_2)OH$, $-CH(C{\equiv}CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NH$aryl, $-(CH_2)_p$-OR^{12}, and $-(CH_2)_p$-SR^{12};

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not –H or alkyl;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl; and

R^{12} is selected from the group consisting of -H, and lower acyl.

60. The method of claim 59 wherein MH or MPO_3^{2-} is selected from the group consisting of LdC, LdT, araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L FddC, L-d4C, L-Fd4C, 3TC, ribavirin, 5-fluoro 2'deoxyuridine, FIAU, FIAC, BHCG, L FMAU, BvaraU, E-5-(2-bromovinyl-2' deoxyuridine, TFT, 5-propynyl-1 arabinosyluracil, CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC, 5-yl-carbocyclic 2'deoxyguanosine, oxetanocin A, oxetanocin G, Cyclobut A, Cyclobut G, dFdC, araC, bromodeoxyuridine, IDU, CdA,

FaraA, Coformycin, 2'-deoxycoformycin, araT, tiazofurin, ddAPR, 9-(arabinofuranosyl)-2,6 diaminopurine, 9-(2'-deoxyribofuranosyl)-2,6 diaminopurine, 9-(2'-deoxy 2'fluororibofuranosyl)-2,6-diaminopurine, 9 (arabinofuranosyl)guanine, 9-(2' deoxyribofuranosyl)guanine, 9-(2'-deoxy 2'fluororibofuranosyl)guanine, FMdC, 5,6 dihydro-5-azacytidine, 5-azacytidine, 5-aza 2'deoxycytidine, AICAR, ACV, GCV, penciclovir, (R)-9-(3,4 dihydroxybutyl)guanine, and cytallene.

61. The method of claim 58 wherein MPO_3^{2-} is selected from the group consisting of PMEA, PMEDAP, HPMPC, HPMPA, FPMPA, and PMPA.

62. The method of claim 58 wherein MPO_3^{2-}, $MP_2O_6^{3-}$, or $MP_3O_9^{4-}$ is useful for the treatment of diseases of the liver or metabolic diseases where the liver is responsible for the overproduction of a biochemical end product.

63. The method of claim 62 wherein said disease of the liver is selected from the group consisting of diabetes, hepatitis, cancer, fibrosis, malaria, gallstones, and chronic cholecystalithiasis.

64. The methods of claim 63 wherein MPO_3^{2-}, $MP_2O_6^{3-}$, or $MP_3O_9^{4-}$ is an antiviral or anticancer agent.

65. The method of claim 62 wherein said metabolic disease is selected from the group consisting of diabetes, atherosclerosis, and obesity.

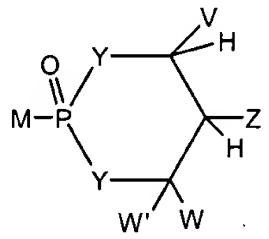
66. The method of claim 62 wherein said biochemical end product is selected from the group consisting of glucose, cholesterol, fatty acids, and triglycerides.

67. The method of claim 66 wherein MPO_3^{2-} is an AMP activated protein kinase activator.

68. The method of claim 58 wherein said oral bioavailability is at least 10%.

69. The method of claim 58 wherein said oral bioavailability is enhanced by 50% compared to the parent drug administered orally.

70. A method of delivering a biologically active drug to an animal for a sustained period using compounds of formula I:



I

wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is independently selected from the group consisting of -O-, $-NR^6-$ with the proviso that at least one Y is $-NR^6-$;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent, but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

1) M is not –NH(lower alkyl), -N(lower alkyl)$_2$, -NH(lower alkylhalide), –N(lower alkylhalide)$_2$, or –N(lower alkyl) (lower alkylhalide); and

2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

71. The method of claim 70 wherein M is attached to the phosphorus in formula I via an oxygen atom or a carbon atom; wherein

V, W, and W' are independently selected from the group consisting of -H, alkyl, aryl, substituted aryl, heteroaryl, and substituted heteroaryl, or

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from an O attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2$NHaryl, $-(CH_2)_p$-OR^{12}, and $-(CH_2)_p$-SR^{12};

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not –H or alkyl;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{12} is selected from the group consisting of -H, and lower acyl.

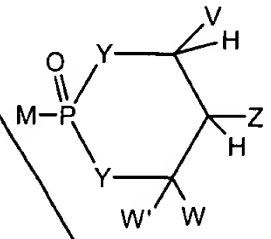
72. The method of claim 71 wherein MH or MPO_3^{2-} is selected from the group consisting of LdC, LdT, araA, AZT, d4T, ddI, ddA, ddC, L-ddC, L FddC, L-d4C, L-Fd4C, 3TC, ribavirin, 5-fluoro 2'deoxyuridine, FIAU, FIAC, BHCG, L FMAU, BvaraU, E-5-(2-bromovinyl-2' deoxyuridine, TFT, 5-propynyl-1 arabinosyluracil, CDG, DAPD, FDOC, d4C, DXG, FEAU, FLG, FLT, FTC, 5-yl-carbocyclic 2'deoxyguanosine, oxetanocin A,

oxetanocin G, Cyclobut A, Cyclobut G, dFdC, araC, bromodeoxyuridine, IDU, CdA, FaraA, Coformycin, 2'-deoxycoformycin, araT, tiazofurin, ddAPR, 9-(arabinofuranosyl)-2,6 diaminopurine, 9-(2'-deoxyribofuranosyl)-2,6 diaminopurine, 9-(2'-deoxy 2'fluororibofuranosyl)-2,6-diaminopurine, 9 (arabinofuranosyl)guanine, 9-(2' deoxyribofuranosyl)guanine, 9-(2'-deoxy 2'fluororibofuranosyl)guanine, FMdC, 5,6 dihydro-5-azacytidine, 5-azacytidine, 5-aza 2'deoxycytidine, AICAR, ACV, GCV, penciclovir, (R)-9-(3,4 dihydroxybutyl)guanine, cytallene PMEA, PMEDAP, HPMPC, HPMPA, FPMPA, PMPA, foscarnet, and phosphonoformic acid.

73. The method of claim 70 whereby therapeutic levels of said drug are maintained for at least one hour longer than the levels achieved by oral administration of the bispivaloyloxymethyl (bis-POM) ester.

74. The method of claim 70 wherein MH or MPO_3^{2-} is an antiviral or anticancer agent.

75. A method of delivering a biologically active drug to an animal with greater selectivity for the liver using compounds of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy,

alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is independently selected from the group consisting of -O-, $-NR^6-$ with the proviso that at least one Y is $-NR^6-$;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent, but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

1) M is not –NH(lower alkyl), -N(lower alkyl)$_2$, -NH(lower alkylhalide), -N(lower alkylhalide)$_2$, or –N(lower alkyl) (lower alkylhalide); and

2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

76. The method of claim 75 whereby the ratio of a parent drug or a drug metabolite concentration in the liver over a parent drug or a drug metabolite concentration in the plasma is two times greater compared to administration of a parent drug.

77. The method of claim 76 wherein the liver specificity has increased relative to administration of M-PO_3^{2-}.

78. The method of claim 75 wherein said biologically active drug is a triphosphate generated in the liver.

79. The method of claim 78 wherein MH is selected from the group consisting of araA, AZT, d4T, 3TC, 1-β-D-ribofuranosyl-1,2,4-triazole-3-carboxamide, ACV, 9-(4-hydroxy-3-hydroxymethylbut-1-yl)guanine, 5-yl-carbocyclic 2'-deoxyguanosine, dFdC, araC, F-ara-A, FTC, and CdA.

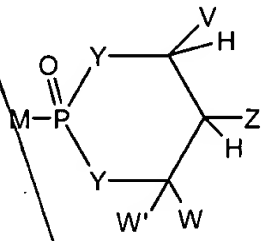
80. The method of claim 75 wherein the active drug is MPO_3^{2-}.

81. The method of claim 80 wherein the drug is selected from the group consisting of FdUMP.

82. The method of claim 75 wherein the active drug is $MP_3O_9^{4-}$ and M is attached via carbon.

83. The method of claim 82 wherein the parent drug MPO_3^{2-} is PMEA; PMEDAP; HPMPC, HPMPA; FPMEA; PMPA foscarnet, and phosphoracetic acid.

84. A method of increasing the therapeutic index of a drug by administering to an animal compounds of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is independently selected from the group consisting of -O-, $-NR^6-$ with the proviso that at least one Y is $-NR^6-$;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent, but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

1) M is not –NH(lower alkyl), -N(lower alkyl)$_2$, -NH(lower alkylhalide), –N(lower alkylhalide)$_2$, or –N(lower alkyl) (lower alkylhalide); and

2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

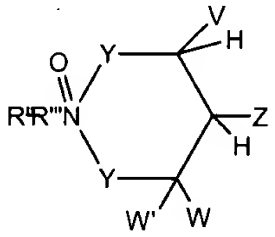
85. The method of claim 84 wherein extrahepatic toxicity is reduced.

86. The method of claim 85 wherein M-PO_3^{2-} is excreted by the kidney.

87. The method of claim 85 wherein the gastrointestinal toxicity is reduced.

88. The method of claim 85 wherein central or peripheral nervous system toxicity is reduced.

89. A method of bypassing kinase resistance by administering to an animal compounds of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, $-CH(aryl)OH$, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is independently selected from the group consisting of -O-, $-NR^6-$ with the proviso that at least one Y is $-NR^6-$;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent, but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

1) M is not –NH(lower alkyl), $-N(\text{lower alkyl})_2$, -NH(lower alkylhalide), $-N(\text{lower alkylhalide})_2$, or –N(lower alkyl) (lower alkylhalide); and

2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

90. The method of claim 89 wherein said resistance arises from the absence or low levels of enzymes responsible for phosphorylating MH.

91. The method of claim 89 wherein said resistance arises from inadequate cellular production of M-PO_3^{2-}.

92. The method of claim 89 wherein said compound is an anticancer or antiviral agent.

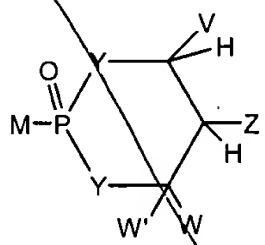
93. The method of claim 92 wherein MH is F-ara-A, araC, CdA, dFdc, and 5-fluoro-2'-deoxyuridine.

94. The method of claim 92 wherein said resistance is to an antiviral agent selected from the group consisting of LdC, LdT, araA, AZT, d4T, 3TC, ribavirin, 5 fluoro-2'deoxyuridine, FMAU, DAPD, FTC, 5-yl-carbocyclic 2'deoxyguanosine, Cyclobut G, dFdC, araC, IDU, FaraA, ACV, GCV, DXG, and penciclovir.

95. The method of claim 92 wherein the resistance or lack of antihepatitis activity is due to a deficiency in thymidine kinase and said antiviral agent is selected from the group consisting of AZT, d4T, and ACV.

96. The method of claim 92 wherein said anticancer agent is selected from the group consisting of dFdC, araC, F-araA, and CdA.

97. A method of treating cancer expressing a P450 enzyme, by administering to an animal a compound of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

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Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is independently selected from the group consisting of -O-, $-NR^6-$ with the proviso that at least one Y is $-NR^6-$;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent, but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

1) M is not –NH(lower alkyl), -N(lower alkyl)$_2$, -NH(lower alkylhalide), –N(lower alkylhalide)$_2$, or –N(lower alkyl) (lower alkylhalide); and

2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

98. The method of claim 97 wherein said cancer is hepatocellular carcinoma.

99. The method of claim 97 wherein the active drug is the triphosphate of M-H.

100. The method of claim 97 wherein the active drug is the monophosphate of M-H.

101. The method of claim 97 wherein said prodrug is administered to patients resistant to the parent drug.

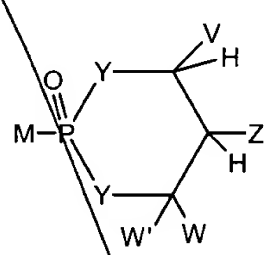
102. The compounds of claim 1 wherein R^6 is lower alkyl.

103. The compounds of claim 102 wherein R^6 is methyl.

104. The method of claim 100 wherein MH is selected from the group consisting of F-araA, araC, CdA, dFdc, and 5-fluoro-2'-deoxyuridine.

105. The method of claim 97 wherein MH is selected from the group consisting of dFdC, araC, FaraA, CdA, 5-fluoro 2'deoxyuridine, GCV, tiazofurin, IDU, 5,6 dihydro-5-azacytidine, 5-azacytidine, and 5-aza 2'deoxycytidine.

106. A method of treating liver fibrosis by administering to an animal a compound of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH{=}CR^2_2)OH$, $-CH(C{\equiv}CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NH$aryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is independently selected from the group consisting of -O-, $-NR^6-$ with the proviso that at least one Y is $-NR^6-$;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent, but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

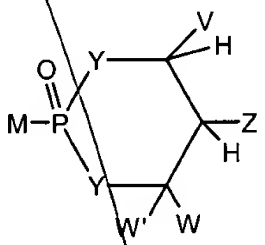
with the provisos that:

1) M is not –NH(lower alkyl), -N(lower alkyl)$_2$, -NH(lower alkylhalide), –N(lower alkylhalide)$_2$, or –N(lower alkyl) (lower alkylhalide); and

2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

107. A method of treating hyperlipidemia by administering to an animal a compound of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy,

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alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is independently selected from the group consisting of -O-, $-NR^6-$ with the proviso that at least one Y is $-NR^6-$;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent, but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

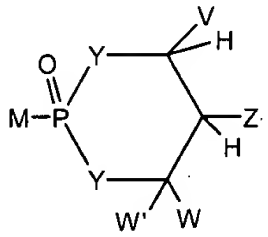
1) M is not –NH(lower alkyl), -N(lower alkyl)$_2$, -NH(lower alkylhalide), –N(lower alkylhalide)$_2$, or –N(lower alkyl) (lower alkylhalide); and

2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

108. The method of claim 107 wherein the hyperlipidemia agent is a squalene synthase inhibitor.

109. A method of treating parasitic infections by administering to an animal a compound of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is independently selected from the group consisting of -O-, $-NR^6-$ with the proviso that at least one Y is $-NR^6-$;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent, but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

1) M is not –NH(lower alkyl), -N(lower alkyl)$_2$, -NH(lower alkylhalide), –N(lower alkylhalide)$_2$, or –N(lower alkyl) (lower alkylhalide); and

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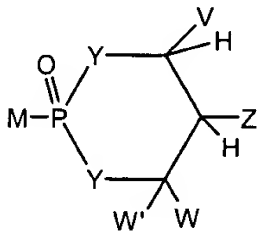
2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

110. A method of delivering diagnostic imaging agents to the liver comprising administration to an animal of compound of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is independently selected from the group consisting of -O-, $-NR^6-$ with the proviso that at least one Y is $-NR^6-$;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent, but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

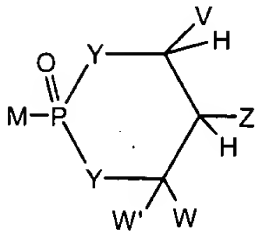
1) M is not –NH(lower alkyl), $-N(\text{lower alkyl})_2$, -NH(lower alkylhalide), $-N(\text{lower alkylhalide})_2$, or –N(lower alkyl) (lower alkylhalide); and

2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

111. The method of claim 110 wherein MH is IDU.

112. A method of treating viral infections by administering to an animal a compound of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2aryl$, -CH(aryl)OH, $-CH(CH{=}CR^2_2)OH$, $-CH(C{\equiv}CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is independently selected from the group consisting of -O-, $-NR^6-$ with the proviso that at least one Y is $-NR^6-$;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent, but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

1) M is not –NH(lower alkyl), $-N(\text{lower alkyl})_2$, -NH(lower alkylhalide), $-N(\text{lower alkylhalide})_2$, or –N(lower alkyl) (lower alkylhalide); and

2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

113. The method of claim 112 wherein said viral infection is hepatitis.

114. The method of claim 113 wherein MH is selected from the group consisting of lobucovir, FTC, 3TC, BMS 200,475, DAPD, DXG, L-FMAU, LdC, LdT, ribavirin, ACV, GCU, and pencyclovir.

115. The method of claim 113 wherein said prodrug is administered to patients resistant to the parent drug.

116. The method of claim 112 wherein said hepatitis is hepatitis B.

117. The method of claim 112 wherein said hepatitis is hepatitis C.

118. The methods of claim 112 wherein viral kinases produce $M\text{-}PO_3^{2-}$.

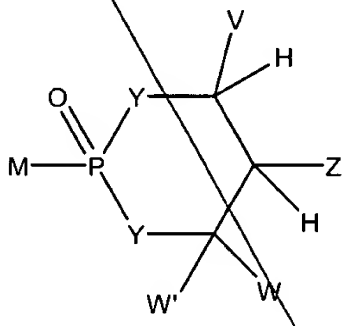
119. The method of claim 118 wherein said viral infection is hepatitis and said viral kinases are kinases from viruses other than the hepatitis viruses.

120. The method of claim 112 wherein the active drug is the triphosphate of M-H.

121. A method of delivering a biologically active drug to target tissues comprising:

a) enhancing the activity of a P450 enzyme that oxidizes the compounds of formula I in said target tissues; and

b) administering to an animal a compound of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

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R^6 is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is independently selected from the group consisting of –O-, -NR^6- with the proviso that at least one Y is –NR^6-;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, $P_3O_9^{4-}$, or $P(O)(NHR^6)O^-$ is a biologically active agent, but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

1) M is not –NH(lower alkyl), -N(lower alkyl)$_2$, -NH(lower alkylhalide), –N(lower alkylhalide)$_2$, or –N(lower alkyl) (lower alkylhalide); and

2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

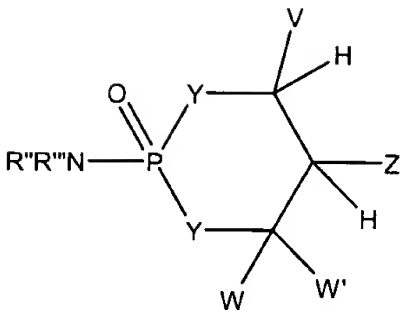
122. The method of claim 121 wherein the activity of a P450 enzyme is enhanced by administering genes that encode a P450 enzyme.

123. The method of claim 121 wherein said activity of P450 enzymes is enhanced by delivering to said target tissue, cells engineered to express P450 enzymes.

124. The method of claim 121 wherein said P450 enzyme activity is enhanced by administration of a compound that increases the amount of engodenous P450 enzyme.

125. The method of claim 124 wherein said compound that increases the amount of endogenous P450 enzyme is selected from the group consisting of phenobarbitol, dexamethasone, rifampicin, phentoin, and preganolon-16α-carbonitrile.

126. A method of treating tumor cells expressing a P450 enzyme comprising administering a cyclophosphamide analog selected from the group consisting of



wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$,

$-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NH$aryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{66} is selected from the group consisting of -H, lower 2-haloalkyl, and lower alkyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

R" is lower 2-haloalkyl;

R"' is selected from the group consisting of H, lower alkyl, and R";

each Y is independently selected from the group consisting of -O-, $-NR^{66}-$ with the proviso that at least one Y is $-NR^{66}-$;

and pharmaceutically acceptable prodrugs and salts thereof.

127. The method of claim 126 wherein said tumor cell is hepatocellular carcinoma.

128. The method of claim 127 wherein R" is 2-chloroethyl, and R"' is selected from the group consisting of –H, and 2-chloroethyl.

129. The method of claim 127 wherein R^{66} is selected from the group consisting of –H, CH_3, and 2-chloroethyl.

130. The method of claim 127 wherein Z, W, W', and R^{66} are –H, and R" and R"' are 2-chloroethyl.

131. The method of claim 127 wherein the activity of a P450 enzyme is enhanced by administration of a compound that increases the amount of engodenous P450 enzyme.

132. The method of claim 131 wherein said compound that increases the amount of endogenous P450 enzyme is selected from the group consisting of phenobarbitol, dexamethasone, rifampicin, phentoin, and preganolon-16α-carbonitrile.

133. The method of claim 126 wherein V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

134. The method of claim 133 wherein Z, W, W', and R^{66} are –H, and R" and R"' are 2-chloroethyl.

135. The method of claim 133 wherein R"', Z, W, and W' are –H, and R" and R^{66} are 2-chloroethyl.

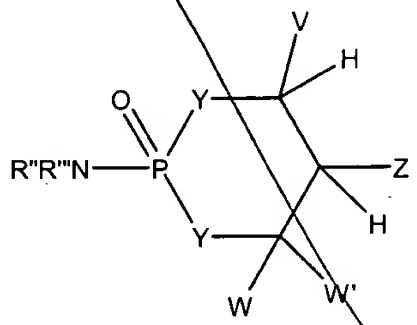
136. The method of claim 133 wherein V is selected from the group consisting of phenyl, 3-chlorophenyl, and 3 bromophenyl.

137. The method of claim 133 wherein V is 4-pyridyl.

138. A method of treating tumor cells comprising

a) enhancing the activity of a P450 enzyme that oxidizes cyclophosphamide analogs;

b) administering to an animal a cyclophosphamide analog selected from the group consisting of:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2$NHaryl, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^{66} is selected from the group consisting of -H, lower 2-haloalkyl, and lower alkyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

R" is lower 2-haloalkyl;

R"' is selected from the group consisting of H, lower alkyl, and R";

each Y is independently selected from the group consisting of -O-, -NR^{66}- with the proviso that at least one Y is -NR^{66}-;

and pharmaceutically acceptable prodrugs and salts thereof.

139. The method of claim 138 wherein the activity of a P450 enzyme is enhanced by administering genes that encode a P450 enzyme.

140. The method of claim 138 wherein said activity of a P450 enzyme is enhanced by delivering to a tumor, cells engineered to express a P450 enzyme.

141. The method of claim 138 wherein said P450 enzyme activity is enhanced by administration of a compound that increases the amount of engodenous P450 enzyme.

142. The method of claim 141 wherein said compound that increases the amount of endogenous P450 enzyme is selected from the group consisting of phenobarbitol, dexamethasone, rifampicin, phentoin, and preganolon-16α-carbonitrile.

143. The method of claim 138 wherein R" is 2-chloroethyl, and R"' is selected from the group consisting of –H, and 2-chloroethyl.

144. The method of claim 138 wherein R^{66} is selected from the group consisting of –H, CH_3, and 2-chloroethyl.

145. The method of claim 138 wherein V is selected from the group consisting of aryl, substituted aryl, heteroaryl, and substituted heteroaryl.

146. The method of claim 145 wherein Z, W, W', and R^{66} are –H, and R" and R"' are 2-chloroethyl.

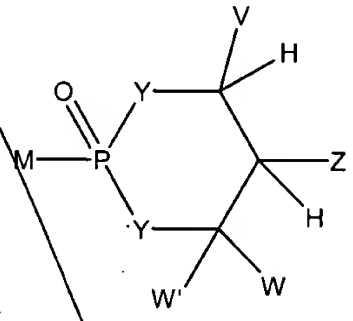
147. The method of claim 145 wherein Z, W, W', and R''' are –H, and R" and R^{66} are 2-chloroethyl.

148. The method of claim 145 wherein V is selected from the group consisting of phenyl, 3-chlorophenyl, and 3 bromophenyl.

149. The method of claim 145 wherein V is 4-pyridyl.

150. A method of making a prodrug of a compound drug having a $-PO_3^{2-}$ or $-P(O)(NHR^6)O^-$ moiety comprising,

a) transforming said phosph(on)ate into a compound of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is independently selected from the group consisting of –O-, $-NR^6-$ with the proviso that at least one Y is $-NR^6-$;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, $P_3O_9^{4-}$, or $P(O)(NHR^6)O^-$ is a biologically active agent, but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

1) M is not –NH(lower alkyl), -N(lower alkyl)$_2$, -NH(lower alkylhalide),

–N(lower alkylhalide)$_2$, or –N(lower alkyl) (lower alkylhalide); and

2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

151. The method of claim 150 further comprising,

a) converting M-PO_3^{2-} to a compound M-P(O)L"$_2$ wherein L" is a leaving group selected from the group consisting of halogen; and

b) reacting M-P(O)L"$_2$ with HY-CH(V)CH(Z)CH(Z)-CW(W')-YH.

152. The method of claim 151 wherein HY-CH(V)CH(Z)-CW(W')-YH is chiral.

153. The method of claim 152 further comprising isolating a single diastereomer.

154. The method of claim 150 wherein

a) converting a hydroxyl or amino to a phosphoramidite by reaction with L-P(-YCH(V)CH(Z)-CW(W')Y-) wherein L selected from the group consisting of NR^1_2, and halogen; and

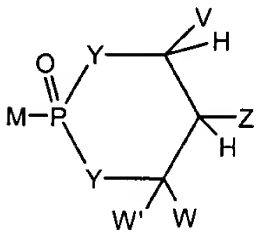
b) transforming said phosphoramidite into a compound of formula I by reaction with an oxidizing agent.

155. The method of claim 154 wherein L-P(-YCH(V)CH(Z)-CW(W')Y-) is chiral.

156. The method of claim 155 wherein the chiral phosphoramidite is generated using a chiral amino alcohol.

157. The method of claim 155 wherein said oxidizing agent produces a single stereoisomer at the phosphorus.

158. The method of making a prodrug of formula I:



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comprising converting a hydroxyl or an amino to a phosphate or phosphoramidate, respectively, by reaction with L'-P(O)(-YCH(V)CH(Z)-CW(W')Y-)

wherein L' is a leaving group selected from the group consisting of $-NR^2_2$, aryloxy, and halogen;

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

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together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, $-CH$(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NH$aryl, $-(CH_2)_p$-OR^{12}, and $-(CH_2)_p$-SR^{12};

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is independently selected from the group consisting of –O-, $-NR^6$- with the proviso that at least one Y is $-NR^6$-.

159. The method of claim 158 wherein L'-P(O)(-YCH(V)CH(Z)-CW(W')Y-) is a single stereoisomer.

160. The method of claim 159 wherein said stereoisomer is generated using a chiral amino alcohol.

161. A compound,

R^1_2N-P-(-YCH(V)CH(Z)-CW(W')Y-)

wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^3$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

q is an integer 1 or 2;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

each R^1 is independently selected from the group consisting of alkyl, aryl, and aralkyl or together R^1 and R^1 form a cyclic group, optionally containing a heteroatom;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is selected from the group consisting of –O- and $–NR^6$- with the proviso that at least one Y is $–NR^6$-.

with the proviso that R^1 is not methyl.

162. A compound $R^1{}_2N$-P(O)(-YCH(V)CH(Z)-CW(W')Y-)

wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $–CHR^2OH$, $-CHR^2OC(O)R^3$,

$-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

q is an integer 1 or 2;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

each R^1 is independently selected from the group consisting of alkyl, aryl, and aralkyl;

or together R^1 and R^1 form a cyclic group, optionally containing a heteroatom;

with the proviso that both R^1 groups are not benzyl or ethyl at the same time; and

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

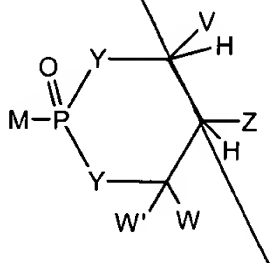
R^6 is selected from the group consisting of -H, lower alkyl, acyloxyalkyl, alkoxycarbonyloxyalkyl, and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is selected from the group consisting of –O- and $–NR^6$- with the proviso that at least one Y is $–NR^6$-.

163. A method of delivering a compound to hepatocytes wherein said compound has a moiety selected from the group consisting of phosph(on)ate comprising:

a) converting said compound to a prodrug of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH=CR^2_2)OH$, $-CH(C\equiv CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is independently selected from the group consisting of -O-, $-NR^6-$ with the proviso that at least one Y is $-NR^6-$;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent, but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

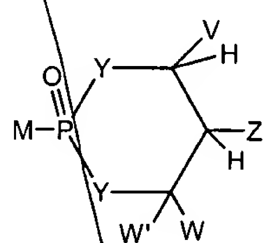
with the provisos that:

1) M is not –NH(lower alkyl), -N(lower alkyl)$_2$, -NH(lower alkylhalide), –N(lower alkylhalide)$_2$, or –N(lower alkyl) (lower alkylhalide); and

2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

164. A method of enhancing the pharmacodynamic half-life of a parent drug by administering to an animal a prodrug of formula I:



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wherein:

V, W, and W' are independently selected from the group consisting of -H, alkyl, aralkyl, alicyclic, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, and 1-alkynyl; or

together V and Z are connected via an additional 3-5 atoms to form a cyclic group containing 5-7 ring atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarbonyloxy, or aryloxycarbonyloxy attached to a carbon atom that is three atoms from both Y groups attached to the phosphorus; or

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together V and Z are connected via an additional 3-5 atoms to form a cyclic group, optionally containing 1 heteroatom, said cyclic group is fused to an aryl group at the beta and gamma position to the Y adjacent to V;

together V and W are connected via an additional 3 carbon atoms to form an optionally substituted cyclic group containing 6 carbon atoms and substituted with one substituent selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, alkylthiocarbonyloxy, and aryloxycarbonyloxy, attached to one of said additional carbon atoms that is three atoms from a Y attached to the phosphorus;

together Z and W are connected via an additional 3-5 atoms to form a cyclic group, optionally containing one heteroatom, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

together W and W' are connected via an additional 2-5 atoms to form a cyclic group, optionally containing 0-2 heteroatoms, and V must be aryl, substituted aryl, heteroaryl, or substituted heteroaryl;

Z is selected from the group consisting of $-CHR^2OH$, $-CHR^2OC(O)R^3$, $-CHR^2OC(S)R^3$, $-CHR^2OC(S)OR^3$, $-CHR^2OC(O)SR^3$, $-CHR^2OCO_2R^3$, $-OR^2$, $-SR^2$, $-CHR^2N_3$, $-CH_2$aryl, -CH(aryl)OH, $-CH(CH{=}CR^2_2)OH$, $-CH(C{\equiv}CR^2)OH$, $-R^2$, $-NR^2_2$, $-OCOR^3$, $-OCO_2R^3$, $-SCOR^3$, $-SCO_2R^3$, $-NHCOR^2$, $-NHCO_2R^3$, $-CH_2NHaryl$, $-(CH_2)_p-OR^{12}$, and $-(CH_2)_p-SR^{12}$;

p is an integer 2 or 3;

with the provisos that:

a) V, Z, W, W' are not all -H; and

b) when Z is $-R^2$, then at least one of V, W, and W' is not -H, alkyl, aralkyl, or alicyclic;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^6 is selected from the group consisting of -H, and lower alkyl, acyloxyalkyl, alkoxycarbonyloxy alkyl and lower acyl;

R^{12} is selected from the group consisting of -H, and lower acyl;

each Y is independently selected from the group consisting of -O-, $-NR^6-$ with the proviso that at least one Y is $-NR^6-$;

M is selected from the group that attached to PO_3^{2-}, $P_2O_6^{3-}$, $P_3O_9^{4-}$ or $P(O)(NHR^6)O^-$ is a biologically active agent, but is not an FBPase inhibitor, and is attached to the phosphorus in formula I via a carbon, oxygen, sulfur or nitrogen atom;

with the provisos that:

1) M is not –NH(lower alkyl), -N(lower alkyl)$_2$, -NH(lower alkylhalide), –N(lower alkylhalide)$_2$, or –N(lower alkyl) (lower alkylhalide); and

2) R^6 is not lower alkylhalide;

and pharmaceutically acceptable prodrugs and salts thereof.

165. The compounds of claim 1 wherein V and M are *cis* to one another on the ring of the prodrug.